developmental time window to initiate lateral compartment differentiation. In the absence of FGF20, lateral compartment cells remain undifferentiated and postmitotic, and unresponsive to Notch-dependent lateral inhibition. The requirement in mice of FGF20 for OC development and hearing, and the lack of other severe phenotypes in the absence of FGF20, suggest that human FGF20 may be a candidate hereditary deafness gene.

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Program/Abstract # 246
The role of Hes/Hey genes in the sensory development of the chicken inner ear
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The Notch pathway plays an essential role in the specification of the prosensory patches and in the determination of hair cells and neurons. The prosensory function of Notch is mediated by Jagged1 (Jag1), which restricts Sox2 expression to the prosensory patches via a mechanism of lateral induction that propagates the Notch signal within the prosensory domains. However, it is not known what couples Notch signaling to lateral induction and Sox2 expression. We have explored the expression patterns of Hes/Hey genes as potential candidates for downstream targets of Notch in the ear. The results show that Hey1 corresponds well with Jag1 expression in the prosensory patches. Hey1 expression is homogeneous within the prosensory patches and parallels lateral induction. On the contrary, Hes5 expression is speckled and delayed with respect to Hey1. It overlaps with Dl1 expression, and both parallel lateral inhibition during neurogenesis and hair cell determination. Hes1 is expressed weakly in sensory patches and Hey2 is mainly expressed in the periotic mesenchyme. The expression of both Hey1 and Hes5 depends on Notch activation and is abolished by DAPT. The forced expression of hJag1 in the otic cup induces Hey1, but not Hes5. After sensory specification, however, hJag1 is unable to induce Hey1 expression outside the sensory domains, suggesting that the competence of the otic epithelium to respond to Notch becomes restricted throughout development. The effect of hJag1 on Hey1 was mimicked by hJag2 but not by cDl1 overexpression. The results suggest that Hey1 is a good candidate to mediate the prosensory function of Notch. Moreover different Notch ligands are associated with different targets and modes of action of Notch.

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Program/Abstract # 247
Sox2 and Ngn1 regulate the neurogenic fate in the developing inner ear
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In the central nervous system (CNS), Sry-related HMG-box 2 (Sox2) is thought to inhibit neurogenesis by keeping neuronal progenitors in an undifferentiated state but its action is counteracted by Ngn2 (Neurogenin 2) to promote neurogenesis. In contrast, over-expression of Sox2 has been shown to promote neurogenesis in mouse cochlear explants. In the developing inner ear, Sox2 is expressed in the neural-sensory competent domain (NSC), but its expression is down-regulated in the neuroblasts that delaminate from the NSC domain to form the cochleovestibular ganglion (CVG). To investigate the role of Sox2 in neurogenesis of the inner ear, we over-expressed Sox2 in the developing chicken inner ears in ovo. Our results indicate that ectopic Sox2 readily induces Neurogenin 1 (Ngn1) expression, an important gene required for the neurogenic fate of the inner ear. Nevertheless, neurogenesis fails to proceed based on the lack of Neurod1 up-regulation and as a result, the size of CVG is reduced. Over-expression of Ngn1 is capable of up-regulation of Neurod1 and causes ectopic neuroblast formation in the otic cup. Similar increases in neurogenesis are obtained with over-expression of Neurod1. Based on these results, we hypothesize that Sox2 is normally involved in initiating neurogenesis by up-regulating Ngn1. The up-regulated Ngn1, in turn, down-regulates Sox2 expression in order for neurogenesis to proceed and Neurod1 to be up-regulated. We provide evidence that Ngn1 inhibits Sox2 expression at the transcriptional level. The inability of Ngn1 to repress the transcription of exogenous Sox2 leads to the failure of neurogenesis in over-expressed Sox2 specimens.

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Program/Abstract # 248
Fate-mapping the vestibular neurogenic region in the developing chicken otic cup using lipophilic dyes
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During inner ear development, precursors of auditory and vestibular neurons delaminate from a neuro-sensory competent domain of the otic cup. This domain eventually gives rise to sensory organs. Previous fate-mapping studies in chicken suggest that precursors of vestibular and auditory neurons are regionally segregated as early as the otic placode stage. This regional organization of the neurogenic region may dictate the type of sensory organs that subsequently form. Here, we show that by the otocyst stage, the Neurod-positive neurogenic domain is delineated by a Crabp1-positive lateral region and a Pax2-positive medial region, which presumably correspond to the areas that give rise to vestibular and auditory neurons, respectively. To verify the neurogenic identity of these two regions, we fate-mapped the presumed vestibular-neurogenic region by focal injections of lipophilic dyes along the lateral edge of the Neurod-positive domain of the otic cup, and follow the labeled cells at the otocyst stage and a later stage when the neurons and sensory organs are differentiated. Our results indicate that labeled cells from the Crabp1-positive lateral region of the neurogenic domain in the otocyst give rise to mostly vestibular neurons. In contrast, labeled cells in a region which weakly expresses both Crabp1 and Pax2 give rise to both vestibular and auditory neurons. Despite the differences in the resulting labeled neurons, the entire lateral edge of the neurogenic domain in the otic cup only label cells within the vestibular sensory organs. The results are consistent with the notion that neuronal fates and subsequent sensory organ types in the inner ear are related.

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Program/Abstract # 249
The role of Hh signaling and proneural genes in otic neurosensory development
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The Role of Hh Signaling and Proneural Genes in Otic Neurosensory Development D. Sapède, S. Dyballa and C. Pujades Department of Experimental and Health Sciences, Universitat Pompeu Fabra, Barcelona, Spain The inner ear is responsible for the perception of motion and sound